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# Low-grade myofibroblastic sarcoma of the distal femur

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ABSTRACT

*INTRODUCTION:* Low-grade myofibroblastic sarcoma (myofibrosarcoma) is described to be a distinct atypical myofibroblastic tumor often with fibromatosis-like features and predilection for head and neck. Low-grade myofibroblastic sarcoma of bone is extremely rare.
*PRESENTATION OF CASE:* A 50-year-old woman was admitted to our hospital because she had experienced right knee pain for 2 years. Plain radiography showed a honeycombed lesion on the right distal femur, and computed tomography showed a bone tumor with cortex destruction invading the soft tissue. A biopsy specimen from the intraosseous lesion showed a hypocellular area of spindle cell proliferation with dense collagen deposition, which is reminiscent of a histological feature of desmoplastic fibroma. However, histological examination of the extraosseous lesion indicated a slightly hypercellular area containing scattered spindle-shaped atypical cells with enlarged nuclei, suggestive of low-grade sarcoma. Spindle-shaped atypical cells were immunohistochemically positive for SMA. A final diagnosis of low-grade myofibroiblastic sarcoma of the bone was made from a surgically resected specimen.
*DISCUSSION:* The patient was alive and well with no evidence of disease at 15 months after the surgery without any additional therapy.
*CONCLUSION:* Extensive sampling of a tumor may be necessary to determine the true nature of the tumor and to make an accurate diagnosis.


## 1. Introduction

Low-grade myofibroblastic sarcoma (myofibrosarcoma) is described to be a distinct atypical myofibroblastic tumor often with fibromatosis-like features and predilection for head and neck.[1] Low-grade myofibroblastic sarcoma of bone is extremely rare, although some predilection for maxilla and mandible has been reported.[2] We encountered a case of low-grade myofibroblastic sarcoma of the right distal femur, which was radiologically and histologically well-documented. Extensive sampling of the tumor was necessary to determine the true nature of the tumor and make an accurate diagnosis.

## 2. Presentation of case

A 50-year-old woman had experienced pain in the right knee for almost 2 years. She was admitted to our hospital because of her knee pain. She had a history of thyroid carcinoma at the age of 30 and uterine leiomyoma. Range of movement of the right knee was full, and the apparent swelling of the distal thigh was not palpated. Upon clinical examination, a tumor was identified on the right distal femur. Plain radiography showed a honeycombed lucent lesion on the right distal femur (Fig. 1A and B). Periosteal reaction was not seen. Computed tomography (CT) showed a bone tumor on the distal femur with cortical thinning, which was partially destroying the cortex and invading the surrounding soft tissue (Fig. 1C). The tumor was restricted in the distal femur, and no lesions suggestive of a metastatic tumor were identified. An incisional biopsy was performed under a clinical diagnosis of desmoplastic fibroma. Biopsy specimens were obtained from both the intraosseous lesion and the soft tissue mass. Histological examination of the intraosseous lesion showed a hypocellular area containing spindle-shaped cells in dense collagen fibers, findings suggestive of desmoplastic fibroma (Fig. 2A). Nuclear atypia of the spindle-shaped cells was mild. However, the specimen from the soft tissue mass exhibited a relatively hypercellular area with a proliferation of atypical spindle-shaped cells. Tumor cells with enlarged hyperchromatic nuclei were occasionally seen, raising the possibility of high-grade sarcoma (Fig. 2B). Immunohistochemistry failed to reveal any specific differentiation including myogenic differentiation. Thus, the possibility of either low-grade fibrosarcoma or high-grade sarcoma was considered on the basis of the biopsy findings. The possibility of low-grade fibrosarcoma, or even high-grade sarcoma, was considered on basis of the biopsy findings. Surgical treatment by wide resection with reconstruction by Kyocera Limb Salvage (KLS) System was performed under the

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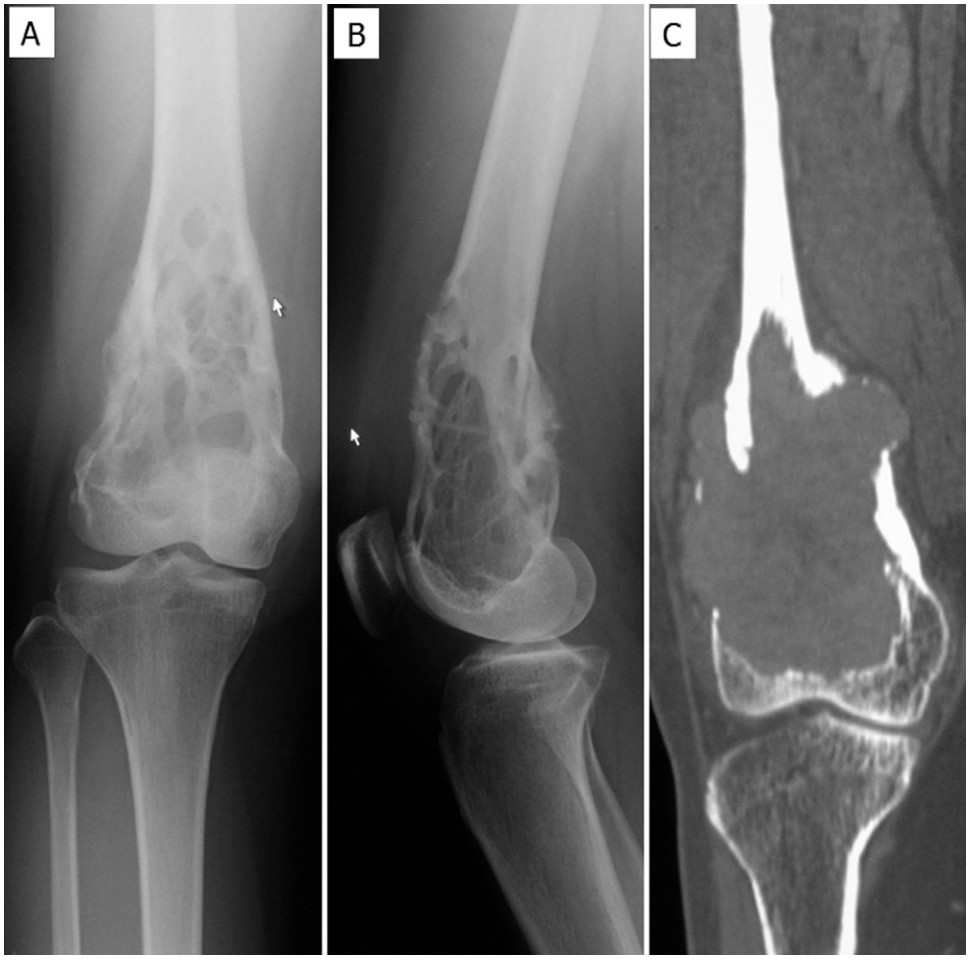


**Fig. 1.** Plain radiograph showing a honeycombed lucent lesion on the right distal femur: (A) anterior-posterior view and (B) lateral view. Computed tomography scan showing a tumor partially destroying the cortex and extending into the surrounding soft tissue (C).

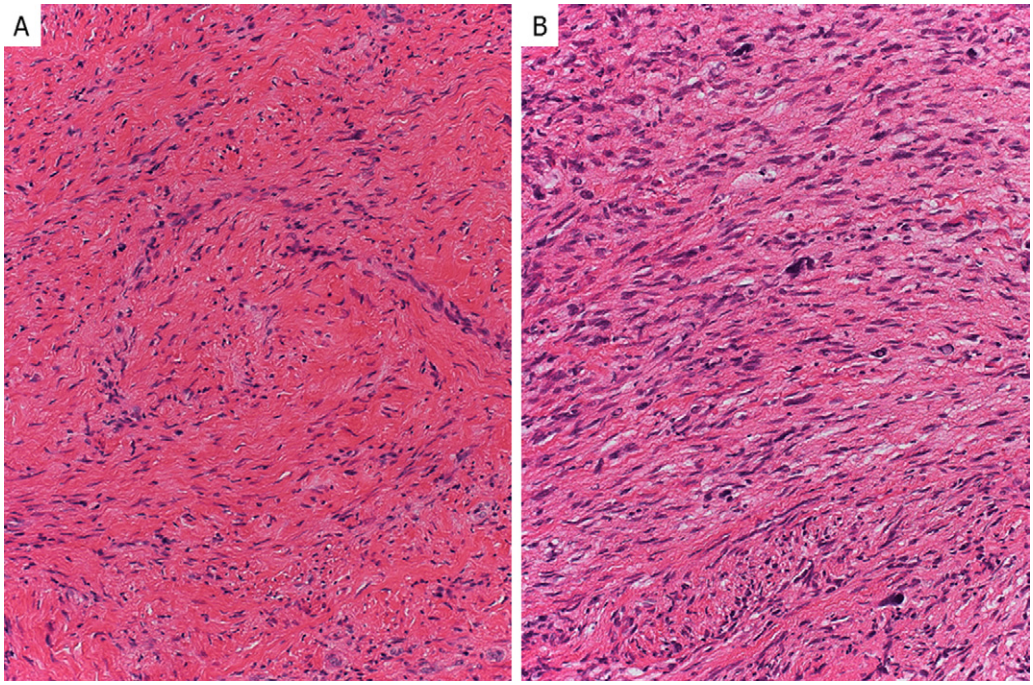


**Fig. 2.** A biopsy from the intraosseous lesion showing a hypocellular area containing a proliferation of spindle cells with abundant intercellular collagen (A, 200×). In contrast, a biopsy from the extraosseous lesion exhibiting a hypercellular area containing a proliferation of spindle cells with hyperchromatic enlarged nuclei on a background of abundant intercellular collagen (B, 200×).

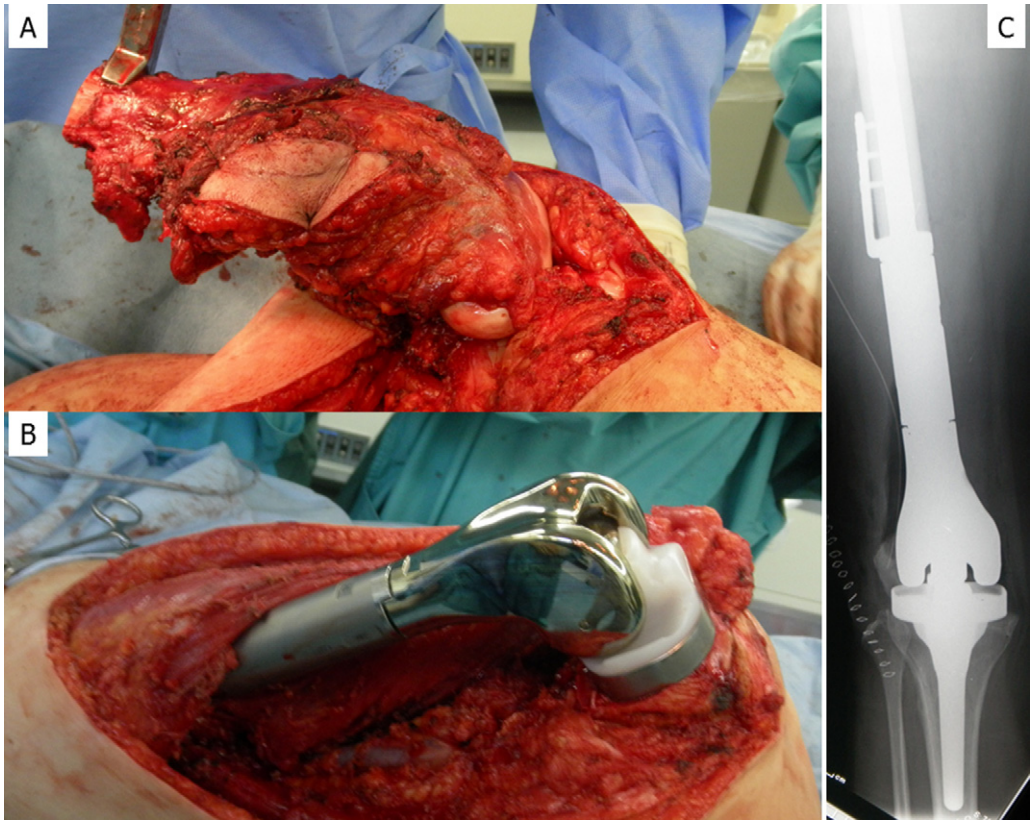


**Fig. 3.** (A) Wide resection was performed. (B) Distal portion of the right femur was replaced by Kyocera Limb Salvage (KLS) System. (C) Post-operative plain radiography shows that distal femur was resected and replaced by prosthesis.

clinical and pathological diagnosis of malignant bone tumor (Fig. 3A–C). The cut surface of the surgically resected tumor was grayish-white. The histological features in the intraosseous lesion of the surgically resected specimen comprised a proliferation of spindle-shaped tumor cells with abundant collagenous fibers (Fig. 4A). Cellularity was relatively low in the intraosseous lesion (Fig. 4B). Some of the spindle-shaped tumor cells contained enlarged atypical nuclei and prominent nucleoli, which were frequently seen in the extraosseous lesion and at the periphery of the intraosseous lesion where the cellularity was relatively high (Fig. 4D and E). The blunt-ended, cigar-shaped cells nuclei characteristics of leiomyosarcoma were not evident, although tumor cells exhibited spindle-shaped morphology. Mitotic figures were seldom seen (less than 1 per 10 high power fields). Tumor necrosis or epithelioid appearance was not observed. Reactive bone formation, but not neoplastic osteoid formation, was observed.

Immunohistochemically, the tumor cells were positive for Vimentin, SMA, and quite focally for M-actin, and negative for desmin and S-100 protein (Fig. 4C and F). MIB-1 labeling index (LI) was less than 1%. We diagnosed this lesion as low-grade myofibroblastic sarcoma of the bone. The patient was alive and well with no evidence of disease at 15 months after the surgery without any additional therapy.

## 3. Discussion

We experienced an extremely rare case of low-grade myofibroblastic sarcoma of the right femur which was successfully treated with wide resection and reconstruction by KLS System. Low-grade myofibroblastic sarcoma preferentially occurs at the extremity and the head and neck region, and low-grade myofibroblastic sarcoma of bone is an extremely rare neoplasm. Watanabe et al. reported 4 cases of low-grade myofibroblastic sarcomas of bone.[3] They described that all tumors were histologically composed principally of a mixture of a cell-rich fascicular area and a hypocellular fibrous area, and that tumor cells with eosinophilic cytoplasm were arranged in weak fascicles in the cellular area.[3] These features are consistent with those of this case.

Myofibroblasts have been characterized as mesenchymal spindle cells sharing both features of fibroblasts and smooth muscle cells. Mentzel et al. characterized myofibrosarcoma or myofibroblastic sarcoma as spindle cell sarcoma composed of myofibroblasts, and described that the myofibroblasts stained positively for at least one of the myogenic markers (desmin, smooth muscle action, muscle actin).[4] Our case showed definite positive staining only for smooth muscle actin among these three myogenic markers.

Differential diagnoses for this tumor include leiomyosarcoma (LMS), low-grade fibrosarcoma, well-differentiated osteosarcoma, desmoplastic fibroma, inflammatory myofibroblastic tumor (IMT), and LMS is a tumor that needs to be most carefully differentiated among them. The classic histologic features of LMS of bone are similar to those of LMS of soft tissue. The tumors are composed of intermingling fascicles of spindle-shaped cells that have a prominent eosinophilic cytoplasm and elongated, blunt-ended nuclei. In this case, spindle-shaped cells with blunt-ended nuclei were not particularly evident. Furthermore, the abundant collagenous stroma in this tumor was unusual for LMS, although it has been reported that the amount of collagen in the stroma in LMS is variable and that the lesion may be focally or diffusely heavily hyalinized.[5] IMT occurs preferentially in the mesentery and retroperitoneum, and is histologically composed of sarcoma-like spindle-shaped cells in the collagenous stroma with massive infiltration of inflammatory cells. In this tumor, inflammatory cells were scarcely seen. Differentiation of desmoplastic fibroma is also difficult especially by small amount of biopsy sample.

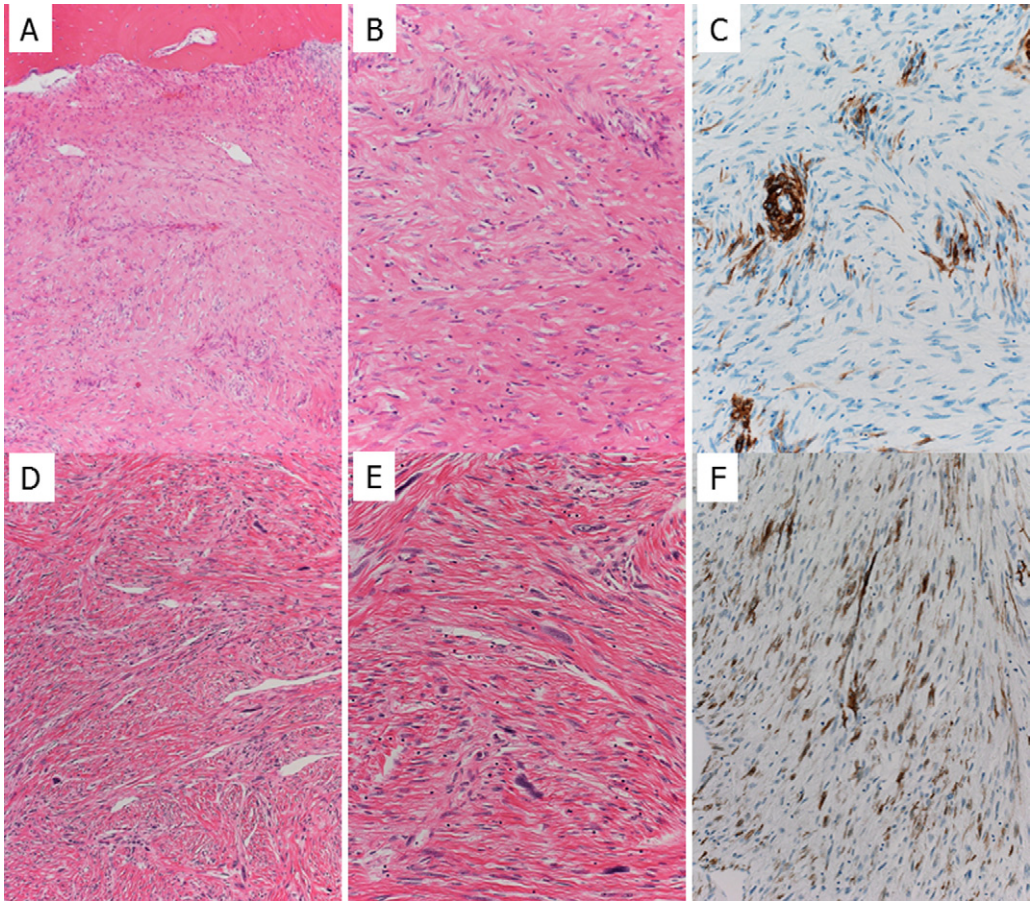


**Fig. 4.** A low-power view of the intraosseous lesion showing a hypocellular area with abundant collagen fibers (A, 100×). Cellular atypia is not evident in the intraosseous component by high-power view (B, 200×). Immunohistochemical examination showing focal positive staining of spindle-shaped tumor cells for smooth muscle actin in the intraosseous lesion (C, 200×). In contrast, a low-power view of the extra-osseous lesion of the surgical specimen showing a cellular area with a proliferation of spindle cells with hyperchromatic enlarged nuclei and eosinophilic cytoplasm (D, 100×). A high-power view of the extraosseous lesion showing frequent atypical cells with enlarged nuclei (E, 200×). Immunohistochemical examination showing positive staining of spindle-shaped tumor cells for smooth muscle actin (F, 200×).

Immunohistochemical analysis of desmoplastic fibroma may reveal the focal expression of SMA.[6] In this case, in addition to the focal expression of SMA in the intraosseous component, diffuse expression of SMA was observed in the extraosseous lesion, which supported the differentiation of spindle-shaped tumor cells into smooth muscle. Furthermore, it is also necessary to detect even scant atypical cells to differentiate malignant tumors including low-grade myofibroblastic sarcoma, LMS and fibrosarcoma of bone from desmoplastic fibroma.[7] In this regard, it is important to obtain sufficient biopsy samples, such as the 2 biopsy samples from both the intraosseous and extraosseous lesions in this case. Insufficient biopsy sampling may lead to misdiagnosis.

The radiologic features of low-grade myofibroblastic sarcoma have not been well-documented, because of its rareness. Watanabe et al. described that all 4 tumors showed osteolytic bone-destructive lesions on plain radiography, and two of which showed definite soft tissue extension.[4] Another case also showed cortical destruction with soft tissue extension.[8] Reactive bone formation was identified 2 out of 4 tumors.[4] In this case, plain radiography showed a honeycombed pattern with a well-defined margin, although cortical destruction with soft tissue extension was observed. We first clinically diagnosed this case as desmoplastic fibroma, because the radiologic appearance of desmoplastic fibromas has been described to be an expansile, lucent lesion with well-defined margins, and a honeycombed pattern is also noted.[5] Infiltrative growth into the soft tissue has been also documented in 48% of desmoplastic fibroma cases.[9]

Regarding the prognosis of low-grade myofibroblastic sarcoma, Montgomery et al. have reported that 4 of 9 low-grade (grade 1) and 3 of 4 intermediate-grade (grade 2) myofibroblastic sarcomas recurred.[10] It has been also reported that the presence of increased proliferative activity and tumor necrosis was associated with more aggressive behavior.[10] In this tumor, mitotic figures were scarcely seen, and MIB-1 LI was less than 1%. In addition, tumor necrosis was not observed. This patient has been well-alive 15 months after surgery without any adjuvant therapy.

## 4. Conclusion

We experienced an extremely rare case of low-grade myofibroblastic sarcoma of the bone. Extensive sampling of the tumor was necessary to determine the true nature of the tumor and make an accurate diagnosis.

## Conflict of interest

All authors disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) our work.

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## Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Authors' contributions

All authors have contributed significantly, and that all authors are in agreement with the content of the manuscript.

Tatsuya Takagi, Tomoaki Torigoe, Taketo Okubo and Kazuo Kaneko performed operation for this case. Tsuyoshi Saito, Hiroyuki Mitomi, and Aiko Kurisaki diagnosed this interesting case. Yoshiyuki Suehara, Tsuyoshi Saito, and Takashi Yao wrote the paper.

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